

### REMARKS

Enclosed is a check for the requisite fee for a three-month extension of time. Any fees that may be due in connection with the filing of this paper or with this application may be charged to Deposit Account No. 06-1050. If a Petition for extension of time is needed, this paper is to be considered such Petition. A supplemental Information Disclosure Statement will be filed under separate cover.

Claims 71, 74, 75 and 79-81 are pending herein. Claim 71 is amended. No new matter is added.

#### **Rejection of claims 71, 74, 75 AND 79-81 Under 35 U.S.C. §103(a)**

Claims 71, 74, 75 and 79-81 are rejected under 35 U.S.C. §103(a) as being unpatentable over Maignan *et al.* (US Pat. No. 4,833,240) because the Examiner alleges that Maignan *et al.* teaches compounds similar to the claimed compounds except that the methano group in the compounds of Maignan *et al.* is substituted by hydrogen. The Examiner alleges that replacing a hydrogen group with an alkyl group on a methano moiety would be an obvious modification to one of ordinary skill in the art. The Examiner also alleges that limiting R''' to be an alkyl would be new matter.

This rejection is respectfully traversed. The allegation that limiting R''' to be an alkyl would be new matter is addressed below in the traverse of the rejection under 35 U.S.C. §112, first paragraph.

#### **RELEVANT LAW**

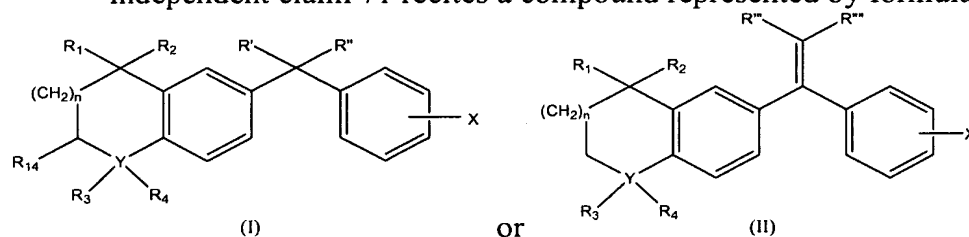
In order to set forth a prima facie case of obviousness under 35 U.S.C. § 103: (1) there must be some teaching, suggestion or incentive supporting the combination of cited references to produce the claimed invention (ACS Hospital Systems, Inc. v. Montefiore Hospital, 732 F.2d 1572, 1577, 221 USPQ 329, 933 (Fed. Cir. 1984)) and (2) the combination of the cited references must actually teach or suggest the claimed invention. Further, that which is within the capabilities of one skilled in the art is not synonymous with that which is obvious. Ex parte Gerlach, 212 USPQ 471 (Bd. APP. 1980). Obviousness is tested by "what the combined teachings of the references would have suggested to those of ordinary skill in the art." In re Keller, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981), but it cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination (ACS Hosp. Systems, Inc. v. Montefiore Hosp. 732 F.2d 1572, 1577. 221 USPQ 329, 933 (Fed. Cir. 1984)). "To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art

reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher" W.L. Gore & Associates, Inc. v. Garlock Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983).

Under 35 U.S.C. §103, in order to set forth a case of prima facie obviousness, the differences between the teachings in the cited reference must be evaluated in terms of the whole invention, and the prior art must provide a teaching or suggestion to the person of ordinary skill in the art to have made the changes that would produce the claimed product. See, e.g., Lindemann Maschinen-fabrik GmbH v. American Hoist and Derrick Co., 730 F.2d 1452, 1462, 221 U.S.P.Q.2d 481, 488 (Fed. Cir. 1984). The mere fact that prior art may be modified to produce the claimed product does not make the modification obvious unless the prior art suggests the desirability of the modification. In re Fritch, 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992); see, also, In re Papesh, 315 F.2d 381, 137 U.S.P.Q. 43 (CCPA 1963). In addition, if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). Moreover, if an independent claim is non-obvious under 35 U.S.C. §103, then claims dependent thereon are also nonobvious. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *see also* MPEP 2143.03.

### The Claims

Independent claim 71 recites a compound represented by formula I or II:



wherein:

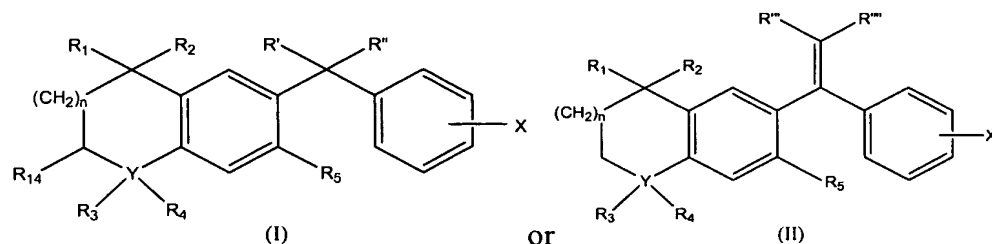
- R<sub>1</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms;
- R<sub>2</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms;
- Y is N, S, or O, wherein:
  - if Y is N, then R<sub>3</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms, and R<sub>4</sub> does not exist,
  - if Y is S, then R<sub>3</sub> does not exist, and R<sub>4</sub> does not exist,
  - if Y is O, then R<sub>3</sub> does not exist, and R<sub>4</sub> does not exist;
- R<sub>14</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms;
- R' is hydrogen or a lower alkyl comprising 1-4 carbon atoms and R'' is a lower alkyl comprising 1-4 carbon atoms;

R''' is hydrogen or a lower alkyl comprising 1-4 carbon atoms, and R'''' is a lower alkyl comprising 1-4 carbon atoms;

X is COOH and originates from C3, C4, or C5 of the ring; and n = 0-1;  
or a pharmaceutically acceptable ester, amide or salt thereof.

Claim 79 is directed to a pharmaceutical composition that includes a compound of claim 71.

Independent claim 74 recites a compound represented by formula I or II:



wherein:

R<sub>1</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms;

R<sub>2</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms;

Y is C, N, S, or O, wherein:

if Y is C, then R<sub>3</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms, and

R<sub>4</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms,

if Y is N, then R<sub>3</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms, and

R<sub>4</sub> does not exist,

if Y is S, then R<sub>3</sub> does not exist, and R<sub>4</sub> does not exist,

if Y is O, then R<sub>3</sub> does not exist, and R<sub>4</sub> does not exist;

R<sub>5</sub> is OR<sub>7</sub>, wherein R<sub>7</sub> is hydrogen or a lower alkyl comprising 1-6 carbon atoms;

R<sub>14</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms;

R' is hydrogen and R'' is hydrogen, or R' and R'' together form an oxo (keto), or a methano;

R''' is hydrogen;

R'''' is hydrogen;

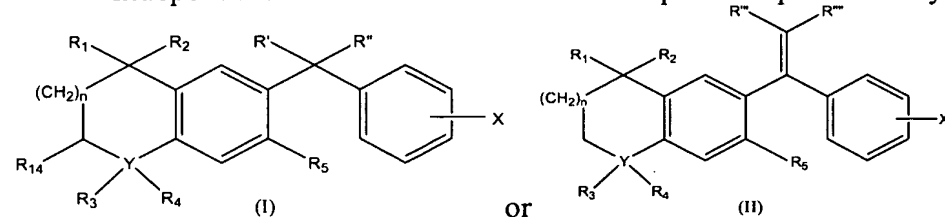
X is COOH and originates from C3, C4, or C5 of the ring; and

n = 0-1; or

a pharmaceutically acceptable ester, amide or salt thereof.

Claim 80 is directed to a pharmaceutical composition that includes a compound of claim 74.

Independent claim 75 is directed to a compound represented by formula I or II:



wherein:

R<sub>1</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms;

R<sub>2</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms;

Y is C, N, S, or O, wherein:

if Y is C, then R<sub>3</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms, and

R<sub>4</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms,

if Y is N, then R<sub>3</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms, and

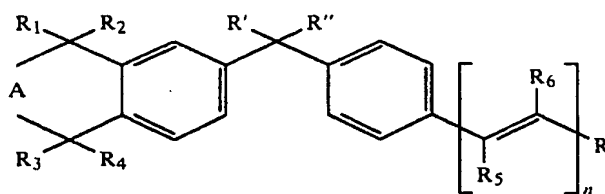
R<sub>4</sub> does not exist,

if Y is S, then R<sub>3</sub> does not exist, and R<sub>4</sub> does not exist,  
if Y is O, then R<sub>3</sub> does not exist, and R<sub>4</sub> does not exist;  
R<sub>5</sub> is OR<sub>7</sub>, wherein R<sub>7</sub> is hydrogen or a lower alkyl comprising 1-6 carbon atoms;  
R<sub>14</sub> is hydrogen or a lower alkyl comprising 1-4 carbon atoms;  
R' is hydrogen or a lower alkyl comprising 1-4 carbon atoms and R'' is a lower alkyl  
comprising 1-4 carbon atoms;  
R''' is hydrogen or a lower alkyl comprising 1-4 carbon atoms, and R'''' is a lower  
alkyl comprising 1-4 carbon atoms;  
X is COOH and originates from C3, C4, or C5 of the ring; and  
n = 0-1; or  
a pharmaceutically acceptable ester, amide or salt thereof.

Claim 81 is directed to a pharmaceutical composition that includes a compound of claim 75.

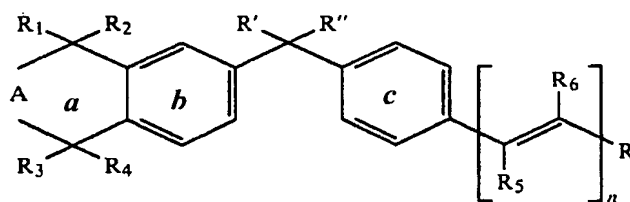
**The Teachings of Maignan *et al.* (US Pat. No. 4,833,240) and differences from the claims**

Maignan *et al.* teaches bicyclic aromatic compounds having the following formula:



Maignan *et al.* teaches that its compounds exhibit an activity in the topical and systemic treatment of dermatological conditions associated with a keratinization disorders, such as differentiation/proliferation, and dermatological conditions having an inflammatory and/or immunoallergic component. Maignan *et al.* teaches that is compounds are used in pharmaceutical or cosmetic preparations.

The ring portions of the compounds of Maignan *et al.* are assigned the following designations for ease of discussion:



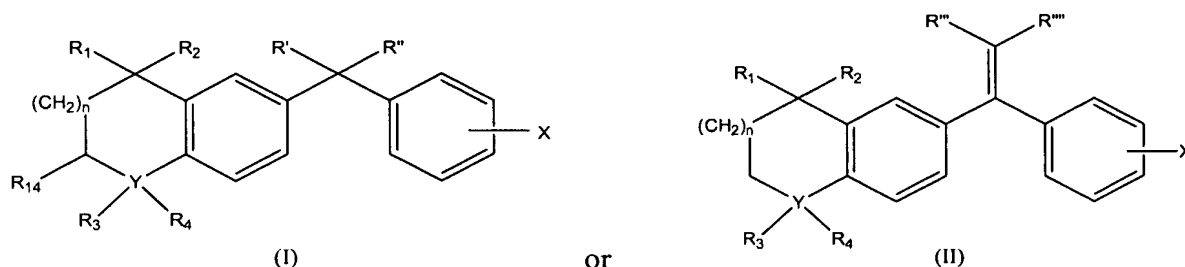
The compounds of Maignan *et al.* differ from the instantly claimed compounds in several aspects. Maignan *et al.* does not teach or suggest any compounds having a nitrogen, sulfur or oxygen atom at the position in ring *a* corresponding to substituent Y in formulae I and II of claim 71. Maignan *et al.* does not teach or suggest any compounds having an -OH or -O(C<sub>1</sub>-C<sub>6</sub>-alkyl) substituent at position 3 of the bicyclic system.

## ANALYSIS

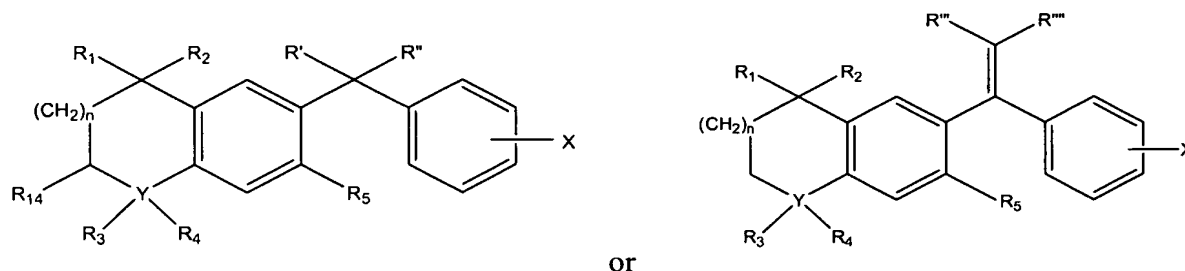
It is respectfully submitted that the Examiner has failed to set forth a case of *prima facie* obviousness because of the following reasons. In particular, the compounds taught by Maignan *et al.* do not encompass any of the instantly claimed compounds nor is their overlap in the general formulae. In addition, none of the compounds of Maignan *et al.* are homologs of any of the compounds as claimed herein.

### 1. Examiner's Characterization of the claimed subject matter is incorrect

As a preliminary matter, Applicant respectfully submits that the Examiner's characterization of the claimed subject matter as set forth on pages 2-3 of the Office Action that the instant claims are drawn to compounds of formula



is not correct. Applicant respectfully submits that independent claims 74 and 75 and claims depending therefrom are drawn to compounds which include substituent  $R_5$  at the 3-position of the bicyclic portion of the compound, as shown in the formula:



where  $R_5$  is  $OR_7$ , where  $R_7$  is hydrogen of a lower alkyl including 1-6 carbon atoms.

### 2. The instantly claimed compounds are not homologs of the compounds described in Maignan *et al.*

#### a. Independent Claim 71

The Examiner alleges that the instant compounds differ from those taught in Maignan *et al.* only in that the instant compounds replace the hydrogen atoms of the methano group bridging rings *b* and *c* of Maignan *et al.* with substituents  $R'''$  and  $R''''$ , where  $R'''$  is hydrogen or an alkyl group and  $R''''$  is an alkyl group. The Examiner alleges that replacing a hydrogen atom in the compounds of Maignan *et al.* with an alkyl group would be obvious to one of

ordinary skill in the art. Hence, it appears that the Examiner is urging that the instantly claimed compounds are homologs of the compounds described in Maignan *et al.*

The Applicant respectfully disagrees. Claim 71 is directed to compounds of formula I or II where substituent Y is selected from among N, S or O. All of the compounds of Maignan *et al.* have a carbon atom at the position in ring *a* corresponding to substituent Y in the compounds of claim 71. Thus, as amended, the compounds of claim 71 are not homologs of the compounds of Maignan *et al.* Maignan *et al.* does not teach or suggest any compounds having a nitrogen, sulfur or oxygen atom at the position in ring *a* corresponding to substituent Y in formulae I and II of claim 71. Maignan *et al.* provides no teaching or suggestion for substituting a nitrogen, sulfur or oxygen atom for the carbon atom at the position in ring *a* corresponding to substituent Y in the compounds of claim 71.

Thus, because the compounds of claim 71 are not homologs of the compounds described in Maignan *et al.*, even if one of ordinary skill in the art modified the compounds of Maignan *et al.* by replacing a hydrogen atom on the methano group bridging the *b* and *c* rings with an alkyl group, such modification would not result in the compounds of claim 71. Hence, the Examiner has failed to set forth a *prima facie* case of obviousness.

b. Independent Claims 74 and 75

The Examiner alleges that the instant compounds differ from those taught in Maignan *et al.* only in that the instant compounds replace the hydrogen atoms of the methano group bridging rings *b* and *c* of Maignan *et al.* with substituents R''' and R''', where R''' is hydrogen or an alkyl group and R''' is an alkyl group. The Examiner alleges that replacing a hydrogen atom in the compounds of Maignan *et al.* with an alkyl group would be obvious to one of ordinary skill in the art. Hence, the Examiner is urging that the instantly claimed compounds are homologs of the compounds described in Maignan *et al.*

Applicant respectfully disagrees. The compounds of independent claims 74 and 75 are directed to compounds of formulae I and II, where position 3 of the bicyclic system is substituted with substituent R<sub>5</sub>, where R<sub>5</sub> is OR<sub>7</sub>, where R<sub>7</sub> is hydrogen of a lower alkyl including 1-6 carbon atoms. All of the compounds described in Maignan *et al.* have a hydrogen at position 3 of the bicyclic system. Hence, the compounds of claims 74 and 75 are not homologs of the compounds of Maignan *et al.* Maignan *et al.* does not teach or suggest any compounds having an -OH or -O(C<sub>1</sub>-C<sub>6</sub>-alkyl) at position 3 of the bicyclic system. Maignan *et al.* provides no teaching or suggestion for replacing the hydrogen atom at position

3 with substituent R<sub>5</sub>, where R<sub>5</sub> is OR<sub>7</sub>, where R<sub>7</sub> is hydrogen of a lower alkyl including 1-6 carbon atoms.

Thus, because the instant compounds of claims 74 and 75 are not homologs of the compounds described in Maignan *et al.*, even if one of ordinary skill in the art modified the compounds of Maignan *et al.* by replacing a hydrogen atom on the methano group bridging the *b* and *c* rings with an alkyl group, such modification would not result in the compounds of claims 74 and 75. Hence, the Examiner has failed to set forth a *prima facie* case of obviousness.

#### **REJECTION OF CLAIMS 71, 74, 75 AND 79-81 UNDER 35 U.S.C. §112, FIRST PARAGRAPH - ALLEGED NEW MATTER**

Claims 71, 74, 75 and 79-81 are rejected under 35 U.S.C. §112, first paragraph, allegedly for containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor, at the time the application was filed, had possession of the claimed subject matter. The Examiner alleges that the limitation of R''' to be hydrogen and an alkyl and R'''' to be an alkyl group in amendments filed April 21, 2003, and June 11, 2003, represents a departure from the specification and claims as originally filed. The Examiner alleges that the specification only describes compounds where R''' and R'''' are hydrogen, citing all the examples on pages 13 and 14. This rejection is respectfully traversed.

#### **The Claims**

See related section above.

#### **ANALYSIS**

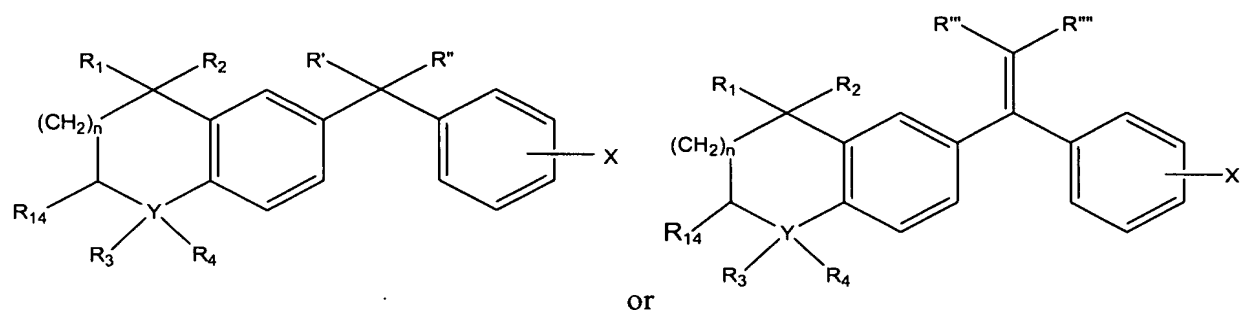
##### 1. Claim 74

Claim 74 does not include as a limitation that R''' is hydrogen or an alkyl and R'''' is an alkyl group. Claim 74 specifies that R''' is hydrogen and R'''' is hydrogen. The Examiner states that the specification discloses compounds where R''' is hydrogen and R'''' is hydrogen (see Office Action, page 4). Thus, as applied to claim 74, the rejection is improper. Claim 80 recites a composition that includes the compounds of claim 74, and thus as applied to claim 80, the rejection is improper. Applicant respectfully requests that the rejection be withdrawn.

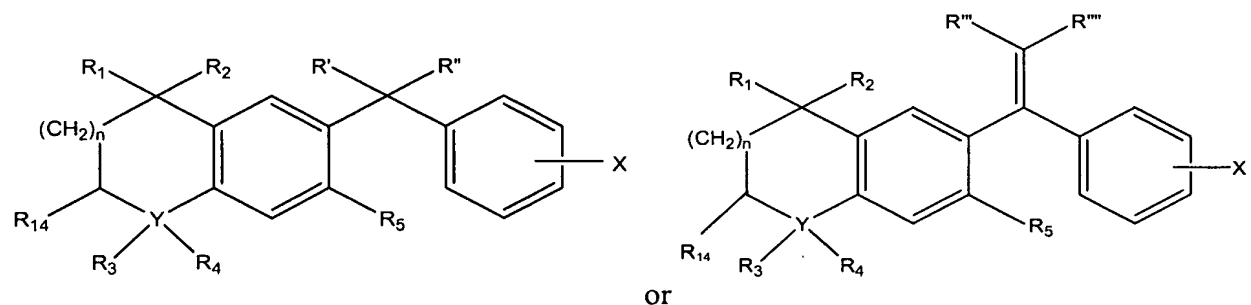
##### 2. Amendment filed April 21, 2003

The amendment stamped by the Tech Center (and entered into PAIR as being filed) on April 21, 2003, did not limit any of the claims to compounds where R''' is "hydrogen and an alkyl" and R'''' is an alkyl group as alleged by the Examiner. In the amendment entered

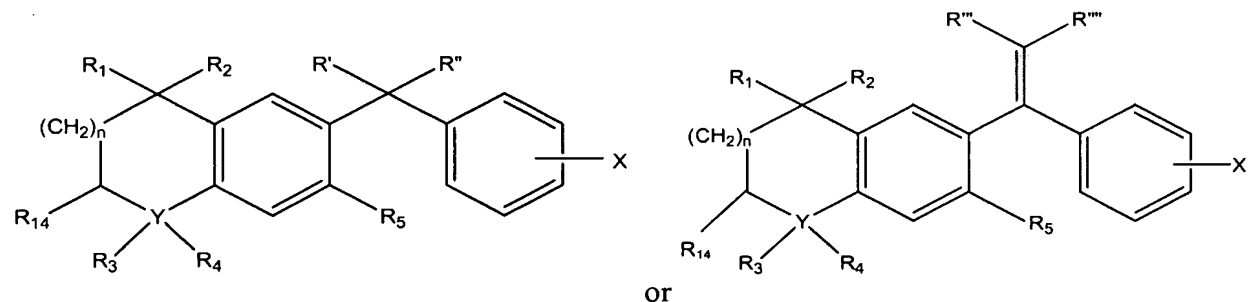
April 21, 2003, new claims 64-70 were submitted. The compounds of claim 64 are of the formulae



where R''' and R'''' each independently represent hydrogen or lower alkyl having 1-4 carbon atoms, but both are not hydrogen. The compounds of claim 65 are of the formulae



where R''' and R'''' represent hydrogen. The compounds of claim 66 are of the formulae



where R''' and R'''' each independently represent hydrogen or lower alkyl having 1-4 carbon atoms, but at least one is not hydrogen, or R''' and R'''' taken together form a cyclopropyl or cycloalkyl group having 3-10 carbons, where the cyclopropyl or cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons. Hence, the amendment entered April 21, 2003 did not limit the substituent R''' to be hydrogen and an alkyl group and the substituent R'''' to be an alkyl group as alleged by the Examiner. Instead, claim 64 recites compounds where R''' and R'''' represent hydrogen and claim 66 recites compounds where R''' and R'''' each independently represent hydrogen or lower alkyl having 1-4 carbon atoms, but at least one is not hydrogen, or R''' and R'''' taken together form a cyclopropyl or cycloalkyl group



having 3-10 carbons, where the cyclopropyl or cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons.

3. Amendment filed June 11, 2003

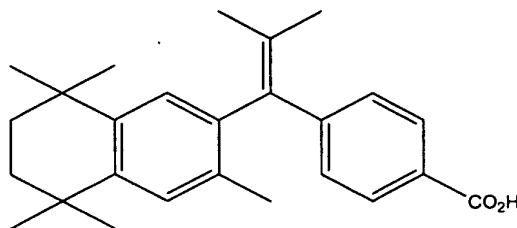
Applicant further respectfully submits that no amendment in this application was mailed by the Applicant or received by the Office on June 11, 2003. Applicant notes that PAIR shows an amendment associated with the date June 11, 2003, but the amendment associated with that date was filed November 6, 2003. The Amendment was transmitted by facsimile under 37 CFR 1.8 on November 6, 2003, and includes an official "received" stamp indicating receipt by the Office at the Central Fax Center on November 6, 2003. Thus, the date of June 11, 2003, in PAIR is an error. The correct date of filing the amendment is November 6, 2003. A copy of the page from PAIR with the official date stamp is provided to evidence the correct date of receipt.

The amendment of November 6, 2003, did not limit any of the claims to compounds where R''' is "hydrogen and an alkyl" and R'''' is an alkyl group as alleged by the Examiner. The amendment filed November 6, 2003, resulted in the cancellation of claims 1-69 and addition of claims 71-81. None of claims 70-81 in the amendment filed November 6, 2003 limits R''' to be "hydrogen and an alkyl" and R'''' to be an alkyl group. As pending on November 6, 2003, Claim 70 does not recite the substituents R''' and R'''. As pending on November 6, 2003, Claims 71 and 75 specify that R''' is hydrogen or a lower alkyl comprising 1-4 carbon atoms and R'''' is a lower alkyl having 1-4 carbon atoms, or R''' and R'''' taken together form a cycloalkyl group comprising 3-10 carbons, where the cycloalkyl group are optionally substituted with a lower alkyl having 1-4 carbons. As pending on November 6, 2003, Claim 74 specifies that R''' is hydrogen and R'''' is hydrogen. Hence, none of the claims pending on November 6, 2003 specify that R''' is hydrogen and an alkyl and R'''' is an alkyl group. Therefore, the Applicant did not limit "the R'" to be hydrogen and an alkyl and R'''' to be an alkyl group" as alleged by the Examiner.

4. Claimed compounds have basis in the original disclosure

Applicant respectfully submits that at the time of application, Applicant appreciated and was in possession of compounds where R''' is hydrogen or a lower alkyl including 1-4 carbon atoms and R'''' is a lower alkyl including 1-4 carbon atoms. The specification provides specific basis for such compounds. For example, see page 11, which discloses that R''' and R'''' represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms. In

addition, see compound 51, which is 4-{1-(3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl)-2-methyl propenyl] benzoic acid, disclosed on page 18, which has the structure:

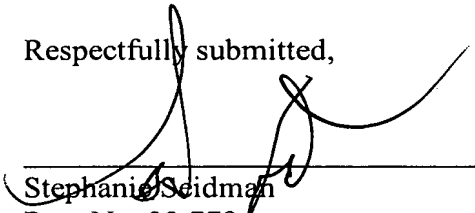


where R''' is a lower alkyl including 1-4 carbon atoms (a methyl group) and R'''' is a lower alkyl including 1-4 carbon atoms (a methyl group). Thus, compounds where R''' is hydrogen or a lower alkyl including 1-4 carbon atoms and R'''' is a lower alkyl including 1-4 carbon atoms have basis in the original disclosure and complies with the written description requirement of 35 U.S.C. §112. Hence, previous amendment of the claims to require R''' to be hydrogen or a lower alkyl including 1-4 carbon atoms and R'''' to be a lower alkyl including 1-4 carbon atoms did not introduce new matter because the specification as filed discloses this embodiment of the claimed subject matter. Therefore, because the claimed compounds are subject matter that is supported by or conforms to the disclosure of the application as filed, the rejection under 35 U.S.C. §112, first paragraph should be withdrawn.

\* \* \*

In view of the above, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,



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